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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,788	11/16/2005	Seishi Kato	2005_1542A	1447

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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
11/04/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/550,788	KATO ET AL.	
	Examiner	Art Unit	
	CYNTHIA B. WILDER	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,11,13-17 and 19* is/are pending in the application.

4a) Of the above claim(s) *11,13-17 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/28/2010 has been entered. Claim 1 has been amended. Claims 6, 8-10, 12 and 18 have been cancelled. Claims 1-5, 7, 11, 13-17 and 19 are pending. Claims 11, 12-17 and 19 are withdrawn from consideration as drawn to a non-elected invention. Claims 1-5 and 7 are discussed below.

New Ground(s) of Rejections

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. It is noted that the cited prior art is deemed acceptable prior art because Applicant has not filed a translation of the prior document filed 3/29/2004). Claims 1-5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chenchik et al (5962271, citation made of record in prior Office action) in view of Brennan et al

(Methods in Enzymology, vol. 100, pages 38-52, 1983). Regarding claim 1, Chenchik et al teach a method comprising the steps of: (i) annealing a double-stranded DNA primer and an mRNA mixture, (ii) preparing an mRNA/cDNA heteroduplex by synthesizing the first-strand cDNA primed with the double-stranded DNA primer using reverse transcriptase, wherein the 3' end nucleotide of the first strand cDNA comprise an anchor (see for example Figure 1), (iii) circularizing the mRNA/cDNA heteroduplex by joining the 3' and 5' ends of the DNA strand containing cDNA using ligase and replacing the RNA in the mRNA/cDNA heteroduplex with the second strand cDNA thereby synthesizing the cDNA (see figure 4-1 and 4-2, col. 3-5, 7-9 and Examples; see also col. 8, line 61 to col. 9, line 13) possessing the 5' end nucleotide cap structure comprising the formula dN_1-dN_2-....dNm-rN_1-rN2....rNn, wherein dN represents a deoxyribonucleotide selected from among dAMP, dCMP, dGMP and dTMP; m represents an integer 0 and above, preferably from 10-50; rN represents a ribonucleotide selected from among AMP, CMP, GMP and UMP, preferably GMP; and n represents an integer 0 and above, preferably from 3 to 7 (col. 3, line 50 to col. 4, line 50).

Chenchick et al do not teach wherein the ligase is T4 RNA ligase, but rather wherein the ligase is T4 DNA ligase.

Brennan et al provide a general teaching T4 RNA ligases. Brennan et al teach that although RNA ligases uses oligoribonucleotides much more efficiently than oligodeoxyribonucleotides, short DNA oligomers can be both circularized and joined imtermolecularly (page 39, second paragraph).

Kato supports the teachings of Brennan by disclosing wherein T4 RNA ligase is used for ligation of DNA-RNA chimeric oligonucleotide to mRNA (col. 3, lines 47-64).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention to substitute T4 RNA ligase as taught by Brennan and Kato in the place of the T4 DNA ligase in the synthesis method of Chenchik since the ordinary artisan has good reasons to peruse the known options within his or her technical grasp and further since the use of T4 RNA ligase does not negatively alter, modify or disrupt the method of synthesis method of Chenchik. In turn, because T4 RNA ligase is known to ligate DNA oligonucleotides, RNA oligonucleotides or chimeric oligonucleotides comprising RNA-DNA to mRNA as taught by Brennan and Kato, one of ordinary skill in the art at the time of the claimed invention could predictably expect a reasonable expectation of success in the DNA synthesis method of Chenchik.

Regarding claim 2, Chenchik et al teach that the small amount of total RNA from 10-50 mg of "difficult" cells or tissues, like human biopsy tissues, pathogenic microorganisms, and tissues at different development stages and so on (col. 11, lines 32-35). One of ordinary skill in the art at the time of the claimed invention would have a reasonable expectation of success in obtaining mRNA contained in a cell extract for use in methods of synthesizing cDNA possessing a cap structured based on the teachings of Chenchik et al. It would have been *prima facie* obvious over the cited prior arts in the absence of secondary consideration.

Regarding claim 3, Chenchik et al teach the method of claim 1, wherein mRNA possessing a cap structure is synthesized by in vitro transcription (col. 5, lines 11-53, and claim 1).

Regarding claim 4, Chenchik et al teach the method of claim 1, wherein the primer sequence of the double-stranded DNA primer contains a sequence complementary to a partial sequence of mRNA possessing a cap structure (see col. 7, line 52 to col. 8, line 43).

Regarding claim 5, Chenchik et al teach the method of claim 1, wherein the primer sequence of the double-stranded DNA primer contains an oligo dT complementary to a poly(A) sequence of mRNA possessing a cap structure (col. 7, lines 50-56).

Regarding claim 7, Chenchik et al teach the method of claim 1, which comprises the following step between the step (ii) and the step (iii): (ii') generating a 5'-protruding end or a blunt end at the terminal of the double-stranded DNA primer by cutting the conjugate of the mRNA/cDNA heteroduplex and the double-stranded DNA primer using a restriction enzyme (col. 11, Example 2).

Response to Arguments

4. Applicant traverses the rejection on the following grounds: Applicant traverses the rejection on the grounds that one could not substitute the T4 RNA ligase of Brennan into the method of Chenchik because the references do not teach wherein the use of T4 ligase is used for ligation of double stranded DNAs.

All of the arguments have been thoroughly reviewed and considered, but it is noted that Applicant provides no evidence to support the conclusions noted above. MPEP states that the arguments of counsel cannot take the place of evidence in the record. *In re Schulze,* 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant (see MPEP 716.01 (b). For these reasons and the reasons already made of record, the rejections are maintained. Additionally, it is again noted that the art supports that DNA can be ligated to DNA using T4 RNA ligase in intramolecular reactions as suggested by Brennan et al. While T4 RNA ligase is not a preferred option for ligating DNA, it does not exclude the fact that T4 RNA ligase can be use to ligate DNA to DNA. Thus, Applicant's arguments are not found persuasive.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-5 and 7 are finally rejected under 35 U.S.C. 103(a) as being unpatentable over Okayama et al (Molecular and Cellular Biology, Feb 1982; citation made of record) in view of Brennan et al (Methods in Enzymology, vol. 100, pages 38-52, 1983). Regarding claim 1, Okayama et al teach a method comprising the steps of: (i) annealing a double-stranded DNA primer and an mRNA mixture, (ii) preparing an mRNA/cDNA heteroduplex by synthesizing the first-strand cDNA primed with the double-stranded DNA primer using reverse transcriptase, (iii) circularizing the mRNA/cDNA heteroduplex by ligating the 5' end of the vector primer to the 3' end of the cDNA using a DNA ligase and replacing the RNA in the mRNA/cDNA heteroduplex with the second strand cDNA thereby synthesizing the cDNA (see figures 1 and 2 and pages 162-165)

Okayama et al do not expressly teach wherein the DNA ligase is a T4 RNA ligase. However, the art teaches that while T4 ligase is preferable for ligating RNA species, it can be use to ligate DNA molecules.

For example, Brennan et al provide a general teaching T4 RNA ligases. Brennan et al teach that although RNA ligases uses oligoribonucleotides much more efficiently than oligodeoxyribonucleotides, short DNA oligomers can be both circularized and joined imtermolecularly (page 39, second paragraph).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the claimed invention to substitute T4 RNA ligase as taught by Brennan and in the place of the T4 DNA ligase in the synthesis method of Okayama et al, since the

ordinary artisan has good reasons to peruse the known options within his or her technical grasp and further since the use of T4 RNA ligase does not negatively alter, modify or disrupt the method of synthesis method of Okayama et al. In turn, because T4 RNA ligase is known to ligate DNA oligonucleotides, RNA oligonucleotides or chimeric oligonucleotides comprising RNA-DNA to mRNA as taught by Brennan, one of ordinary skill in the art at the time of the claimed invention could predictably expect a reasonable expectation of success in the DNA synthesis method of Okayama et al.

Regarding claim 2, Okayama et al teach wherein the mRNA is contained in a cell lysate (page 7, col. 1).

Regarding claim 3, Okayama et al teach the method of claim 1, wherein mRNA is synthesized by in vitro transcription (see materials and Methods, pages 152-164)

Regarding claim 4, Okayama et al teach the method of claim 1, wherein the primer sequence of the double-stranded DNA primer contains a sequence complementary to a partial sequence of mRNA (see Figure 1 and 2).

Regarding claim 5, Okayama et al teach the method of claim 1, wherein the primer sequence of the double-stranded DNA primer contains an oligo dT complementary to a poly(A) sequence of the mRNA (see figure 2).

Regarding claim 7, Okayama et al teach the method of claim 1, which comprises the following step between the step (ii) and the step (iii): (ii') generating a 5'-protruding end or a blunt end at the terminal of the double-stranded DNA primer by cutting the

conjugate of the mRNA/cDNA heteroduplex and the double-stranded DNA primer using a restriction enzyme (see pages 162-165 and Figures 1 and 2).

Conclusion

7. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cynthia B. Wilder/
Examiner, Art Unit 1637